UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,177	07/10/2000	Kuber T. Sampath	CIBT-P02-540	8978

28120 7590 03/18/2003

ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	18

DATE MAILED: 03/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/613,177	Applicant(s) SAMPATH ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13-33 and 36-50* is/are pending in the application.

4a) Of the above claim(s) *14,16-29 and 37-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,15,30-33,36 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

Claims 1-10, 13-33 and 36-50 are pending.

Claims 1-10, 13, 15, 30-33 and 36, 43-50 are rejected.

Claims 14, 16-29 and 37-42 are withdrawn from consideration.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 5, 2003 has been entered.

Double Patenting

2. Claims 1-10, 13, 15, 30-33 and 36, 43-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,834,188. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are a species of the genus of the current claims, where the method of claim 2 of the U.S Patent is drawn to a species of screening using OP-1. The species anticipates the genus claim and renders the genus claim obvious.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim Rejections - 35 USC § 112

The 112, first paragraph and second paragraph rejections are withdrawn in view of the amendments.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Wobus et al (Differentiation (1991) 48:173-182).

Foulkes teaches a method for identifying a compound that induces a biological effect (column 73, lines 40-43), comprising a) providing a test cell comprising a DNA defining a transcription activating element operatively linked to a reporter gene encoding a detectable gene product, which, when present in a responsive cell contacted with a comopund serves to induce transcription of said reporter gene (column 73, lines 44-58), b) exposing said test cell to a candidate compound (column 73, line 59 to column 74, line 5), c) detecting expression of said detectable gene product where the increase in expression of the detectable gene product indicates the ability of the compound to induce the biologic effect (column 73, line 59 to column 74, line 5) and wherein the biological effect requires the presence of the transcription activating element (see, eg. Column 68, lines 10-22, where G-CSF mRNA is increased by the transcription activating element, compounds #542 and #1780). Foulkes expressly teaches producing larger amounts of desirable compounds for use in therapy (column 31).

Foulkes does not teach a motivation to apply the method to differentiated mammalian tissue to identify chronotropic drugs which induce differentiation.

Wobus teaches a motivation to apply the method of Foulkes to the identification of compounds to study differentiation (page 173, column 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes to the screening of compounds which induce differentiated tissue from pluripotent cells as taught by Wobus since Wobus states "The cellular system described may be useful as an in vitro assay for toxicological investigations of chronotropic drugs and a model system for studying committment and cellular differentiation in vitro." (Page 173, column 1). Thus, an ordinary practitioner would have been motivated by Wobus to screen for compounds which are chronotropic, (ie which affect differentiation) and expressly motivated to screen for drugs involved in differentiation.

7. Claims 1-3, 6, 9, 13, 30-33, 36, 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Wobus et al (Differentiation (1991) 48:173-182) and further in view of Nadal-Ginard (WO 94/18239).

Foulkes teaches a method for identifying a compound that induces a biological effect (column 73, lines 40-43), comprising a) providing a test cell comprising a DNA defining a transcription activating element operatively linked to a reporter gene encoding a detectable gene product, which, when present in a responsive cell contacted with a comopund serves to induce transcription of said reporter gene (column 73, lines 44-58), b) exposing said test cell to a candidate compound (column 73, line 59 to column 74, line 5), c) detecting expression of said detectable gene product where the expression indicates the ability of the compound to induce the biologic effect (column 73, line 59 to column 74, line 5). Foulkes expressly teaches producing larger amounts of desirable compounds for use in therapy (column 31). Foulkes teaches the use of vectors with

AP-1 sites such as the CSF-1 promoter which comprises an AP-1 site (column 52, lines 35-60).

Wobus teaches a motivation to apply the method of Foulkes to the identification of compounds to study differentiation (page 173, column 1).

Foulkes does not teach the use of the MEF-2 or AP-1 elements, which are functional in muscle cells.

Nadal-Ginard teaches screening for agents which either enhance of decrease the interaction of MEF2 transcription factors as well as MyoD and MASH transcription factors (abstract).

Further, the sequences of Foulkes, Wobus or Nadal-Ginard are all "variants" of the nucleotides disclosed in claim 30 and meet this limitation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes in view of Wobus to the screening of MEF2 related compounds for the study of differentiated tissue as taught by Nadal-Ginard since Nadal-Ginard states "The agents useful in the invention either enhance or decrease the interaction between a pocket protein, eg retinoblastoma protein and a tissue specific trasncription factor, eg members of the MyoD, MEF2 or MASH family of transcription factors" (abstract)." Nadal-Ginard further notes that "Applicant's discovery provides the basis for screening therapeutic agents useful for regulating the switch between the cell's growth phase and a terminally differentiated state (page 4, lines 18-20)". Thus, an ordinary practitioner would have been motivated by Nadal-Ginard to screen for compounds which are involved in differentiation using the

MEF2 transcription factor sites in view of Nadal-Ginard's express motivation to use these enzymes in screening between differentiation and growth.

8. Claims 1, 13, 36, 43, 45, 46, 47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Smart et al (U.S. Patent 5,650,276).

Foulkes teaches a method for identifying a compound that induces a biological effect (column 73, lines 40-43), comprising a) providing a test cell comprising a DNA defining a transcription activating element operatively linked to a reporter gene encoding a detectable gene product, which, when present in a responsive cell contacted with a comopund serves to induce transcription of said reporter gene (column 73, lines 44-58), b) exposing said test cell to a candidate compound (column 73, line 59 to column 74, line 5), c) detecting expression of said detectable gene product where the increase in expression of the detectable gene product indicates the ability of the compound to induce the biologic effect (column 73, line 59 to column 74, line 5) and wherein the biological effect requires the presence of the transcription activating element (see, eg. Column 68, lines 10-22, where G-CSF mRNA is increased by the transcription activating element, compounds #542 and #1780). Foulkes expressly teaches producing larger amounts of desirable compounds for use in therapy (column 31).

Foulkes does not teach a motivation to apply the method to morphogenesis or morphogen mediated biological effects in order to identify compounds which induce such effects.

Smart teaches "The invention features a method of screening candidate compounds for the ability to modulate the effective local or systemic concentration or level of morphogenic protein in an organism. (see column 2, lines 61-64)." Smart teaches the desirability of screening candidate compounds for their ability to modulate morphogenic proteins (abstract). Smart expressly teaches OP-1 and OP-2 derived from humans (see column 4, line 38). Smart teaches morphogenic effects such as stimulating proliferation of progenitor cells (See column 2, lines 26-59) including osteoblasts (see column 17, lines 35-36).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes to the screening of compounds which induce morphogensis since Smart expressly notes the desirability of screening compounds for their ability to modulate morphogenesis (see column 2, lines 61-64, abstract, column 15, lines 55-64, especially). Further, Foulkes expressly notes that "The present invention provides a method of transcriptionally modulating the expression of a homologous gene-of-interest, the expression of which is associated with a defined physiological or pathological effect within a multicellular organism (see column 22, lines 15-18)". Thus, an ordinary practitioner would have been motivated to apply the method of Foulkes, which studies compounds that are associated with physiological effects to address the morphogenic analysis of Smart. Smart teaches that it is desirable to screen compounds for the physiologic effect of morphogenesis. That is, an ordinary practitioner interested in determining which compounds would effect the physiologic pathway termed morphogenesis as motivated by Smart would have been motivated to

apply the method of Foulkes to this analysis since Foukes expressly suggests analysis of such pathways and since Foulkes clearly indicates that such screening can result in clinical and therapeutic advantages (see columns 3 and 4, especially column 4, lines 18-28).

9. Claims 1-3, 6, 9, 13, 36, 43-47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Smart et al (U.S. Patent 5,650,276) and further in view of Nadal-Ginard (WO 94/18239).

Foulkes in view of Smart teach the limitations of claims 1, 13, 36, 43, 45, 46, 47 and 49 as discussed above. Smart expressly teaches that OP-1 is associated with cels in the muscle (see column 16, lines 31-33).

Foulkes in view of Smart do not teach the use of the MEF-2 or AP-1 elements, which are functional in muscle cells.

Nadal-Ginard teaches screening for agents which either enhance of decrease the interaction of MEF2 transcription factors as well as MyoD and MASH transcription factors (abstract).

Further, the sequences of Foulkes, Smart or Nadal-Ginard are all "variants" of the nucleotides disclosed in claim 30 and meet this limitation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes in view of Smart to the screening of MEF2 related compounds for the study of differentiated tissue as taught by Nadal-Ginard since Nadal-Ginard states "The agents useful in the invention either enhance or decrease the interaction between a pocket protein, eg retinoblastoma

protein and a tissue specific trasncription factor, eg members of the MyoD, MEF2 or MASH family of transcription factors" (abstract)." Nadal-Ginard further notes that "Applicant's discovery provides the basis for screening therapeutic agents useful for regulating the switch between the cell's growth phase and a terminally differentiated state (page 4, lines 18-20)". Thus, an ordinary practitioner would have been motivated by Nadal-Ginard to screen for compounds which are involved in differentiation using the MEF2 transcription factor sites in view of Nadal-Ginard's express motivation to use these enzymes in screening between differentiation and growth.

10. Claims 1, 13, 36, 43, and 45-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Smart et al (U.S. Patent 5,650,276) and further in view of Ozkaynak et al (U.S. Patent 5,652,118).

Foulkes in view of Smart teach the limitations of claims 1, 13, 36, 43, 45, 46, 47 and 49 as discussed above.

Foulkes in view of Smart do not teach the association of N-CAM and morphogenesis.

Ozkaynak expressly teaches screening for candidate compounds which alter endogenous morphogen levels (see example 9, column 37-38) and Ozkaynak expressly teaches the association of N-CAM expression with morphogenesis (see column 29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes in view of Smart to the screening of N-CAM related compounds since Ozkaynak states "The morphogens described herein induce CAM expression, particularly N-CAM expression, as part of

their induction of morphogenesis (see column 29, lines 2-3)" and since Ozkaynak further states the desirability of compound screening in example 9.

Response to Arguments

11. Applicant's arguments filed February 5, 2003, have been fully considered but they are not persuasive.

Applicant first argues that the Foulkes in view of Wobus rejection does not teach a "morphogen mediated biological effect" because the compounds of Wobus teaches screening for chronotropic drugs, which are compounds which induce muscle contraction. However, this argument fails to recognize the scope of the term "morphogen mediated biological effect" as defined by the specification. The specification defines "morphogen mediated biological effect" by stating "The effect can be any biological effect resulting from exposure to or contact with a morphogen (see page 19, lines 9-10). Thus, the claim is broadly permissive to any biological effect, including the chronotropic effect disclosed by Wobus. Thus, contrary to Applicant's argument, all the elements necessary for a prima facie case of obviousness are present.

Applicant then argues the 103 including Nadal-Ginard, again because there is no showing of a "morphogen mediated" effect. Since this term is so broad, as discussed above, to involve any biological effect, the rejection is maintained.

Further, a new set of prior art rejections are added to address the substance of the "morphogen mediated" terminology.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

March 10, 2003